

1000ppm room cleaning, 5) early detection, 6) BioQuell - experimental and 7) outbreak - control antibiotics and soap for hand hygiene.

Prevention of relapses: Avoid "bad" Abx and antiperistaltics; role of probiotics and gastric pH control - unknown.

doi:[10.1016/j.ijid.2008.05.100](https://doi.org/10.1016/j.ijid.2008.05.100)

34.004

Managing CDAD: Current and Upcoming Approaches

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The epidemiology, clinical severity and case-fatality ratio of *Clostridium difficile* infection (CDI) changed dramatically with the emergence of a toxin hyperproducing strain (BI/NAP1/027) in North America and Europe since 2000. These changes have stimulated the quest for novel therapeutic approaches, and a re-examination of the comparative efficacy of metronidazole versus oral vancomycin. Unfortunately, tolevamer, the only novel treatment evaluated so far in phase 3 trials, has proven inferior to comparators, and metronidazole and vancomycin remain the two most commonly used drugs. The major advantage of metronidazole is its low price. The major advantage of orally administered vancomycin lies in its more favorable pharmacokinetics. Facilitating vancomycin-resistant enterococci colonization/infection is a potential drawback of both drugs. The randomized controlled trials published so far used intermediate outcomes rather than outcomes that now preoccupy clinicians: the frequency of complications or recurrences. Pending the development of a prospectively validated scoring system, the IDSA/SHEA expert committee will define severe CDI as any patient with a leukocytosis $\geq 15000/\text{mm}^3$ or a creatinine increased by $\geq 50\%$ from baseline. For patients with mild-to moderate CDI (leukocytosis $< 15000/\text{mm}^3$ and creatinine $< 1.5 \times$ baseline), there is no evidence that vancomycin is superior to metronidazole (even for intermediate outcomes), and metronidazole should be preferred. For patients with severe CDI not infected with BI/NAP1/027, there is reasonable evidence that the better pharmacokinetics of vancomycin translate into a lower probability of complications. For those infected with BI/NAP1/027, the superiority of vancomycin remains to be proven. About one fourth of patients treated with either metronidazole or vancomycin will experience at least one recurrence. There is now some evidence that the more common post-metronidazole recurrences documented recently in some centers may have corresponded to re-infections among patients who remained exposed in the hospital environment.

doi:[10.1016/j.ijid.2008.05.101](https://doi.org/10.1016/j.ijid.2008.05.101)

35.001

HPV Types 16, 18, 45 and 31: The Most Important Oncogenic HPV Types Worldwide

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HPV infections are the most common sexually transmitted infections. HPV types differ in transmission capacity, virulence and in their ability to induce cancer. Over 90% of HPV-attributable cancers in women are cervical cancer. Most cancers of the uterine cervix are squamous cell carcinomas, while adenocarcinoma represents 10-12% of the global cervical cancer burden (in some countries of Europe and North America it amounts to over 20% of all invasive cervical cancer).

On worldwide estimates, HPV-16 is consistently the most common type (60%) in cervical cancer, followed by HPV-18, -45 and -31. These four types combined account for approximately 80% of squamous cell carcinomas and 90% of adenocarcinomas. Some variability in the ranking thereafter has been described.

Infections with HPV-16, -18, or -45 are associated with a higher risk for progression to cancer. The prognosis of HPV-16 and -18 is now being established by cohort studies with 10+ years of follow-up. The probability and time to progression to HSIL among HPV-16 and/or HPV-18 positive women with normal cytology is significantly higher than for any other of the high-risk HPV types, although the estimates for each individual type other than HPV-16 and -18 have not been firmly established.

Adenocarcinoma is not detected effectively by cervical screening and is increasing in incidence in Europe and North America. It is associated with higher recurrence rates and poor outcomes. HPV-18 and -45 account for more than 40% of adenocarcinomas.

Among other HPV positive cancer cases, HPV-16 is the dominant type. HPV-18 and -45 are the next most common types, although the relative role of the remaining HPV types is still to be determined.

In summary, on a worldwide scale, prevention of cervical and other genital cancers would greatly benefit from vaccination focused on HPV-16 and -18.

doi:[10.1016/j.ijid.2008.05.102](https://doi.org/10.1016/j.ijid.2008.05.102)

35.002

The Value of New Adjuvant Technology

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The development of safe and efficacious vaccines against pathogens like malaria, HIV and TB and the induction of protective immune responses in populations with impaired immunity such as the elderly remain major challenges. The growing understanding of the role of the innate immune system in the initial triggering of specific, adaptive immune